

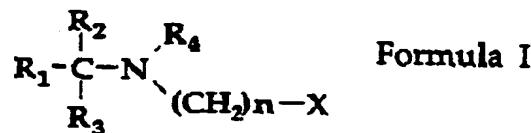
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WE CLAIM:

1. A compound of the Formula I

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wherein:

- R₁ is (CH₂)_mCH₃ where m is 0 or an integer in the range from 1 to 16, or an alkenyl, alkynyl, alkoxy, alkylthio, or alkyl sulfinyl group having from 2 to 17 carbon atoms, wherein R₁ may be optionally substituted with one or 10 more substituents selected from hydroxy, aldehyde, oxo, lower acyloxy, halogen, thio, sulfoxide and sulfone,
- R₂ = H, CH₃ or CH₂CH₃,
- R₃ = H or CH₃,
- R₄ = H or CH₃,
- 15 R₅ = lower alkyl having from 1 to 5 carbon atoms,
- n is an integer in the range from 1 to 3,
- and X is carboxyl (COOH) or carbalkoxy (COOR₅), cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, as a substantially pure enantiomer in the R or S configuration or a pharmaceutically 20 acceptable salt thereof.

2. A compound of the Formula I according to claim 1 wherein:
- R₁ = (CH₂)_mCH₃ where m is 0 or an integer in the range from 1 to 16,
- R₂ = CH₃,
- R₃ = H,
- 25 R₄ = H or CH₃,
- R₅ = lower alkyl having from 1 to 5 carbon atoms,
- n is an integer in the range from 1 to 3,

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and X is carboxyl (COOH) or carbalkoxy (COOR₅), cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, or a pharmaceutically acceptable salt thereof.

3. A compound of the Formula I according to claim 1 wherein:

5 R₁ = (CH₂)_mCH₃ where m is 0 or an integer in the range from 1 to 16,

R₂ = CH₃,

R₃ = H,

R₄ = H or CH₃,

R₅ = lower alkyl having from 1 to 5 carbon atoms,

10 n is an integer in the range from 1 to 3,

and X is carboxyl (COOH) or carbalkoxy (COOR₅) cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, as a substantially pure enantiomer in the R-configuration, or a pharmaceutically acceptable salt thereof.

15 4. A compound of the formula I according to claim 1 wherein:

R₁ = (CH₂)_mCH₃ where m is 0 or an integer in the range from 1 to 16,

R₂ = CH₃,

R₃ = H,

R₄ = H or CH₃,

20 R₅ = lower alkyl having from 1 to 5 carbon atoms,

n is an integer in the range from 1 to 3,

and X is carboxyl (COOH) or carbalkoxy (COOR₅) cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, as a substantially pure enantiomer in the S-configuration, or a pharmaceutically acceptable salt thereof.

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5. A compound according to claim 3, wherein said compound of formula I is selected from the group consisting of:
(R)-3-(2-Heptylamino)propionic acid;

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- (R)-3-(2-Heptylmethylamino)propionic acid;
Methyl (R)-3-(2-heptylamino)propionate;
Methyl (R)-3-(2-heptylmethylamino)propionate;
(R)-2-(2-Pentylamino)acetonitrile;
- 5 (R)-2-(2-Heptylmethylamino)acetonitrile;
(R)-3-(2-Heptylamino)propionitrile;
(R)-3-(2-Heptylmethylamino)propionitrile;
(R)-2-(2-Pentylamino)ethanephosphonic acid;
(R)-2-(2-Heptylmethylamino)ethanephosphonic acid; and
- 10 (R)-2-(2-Heptylamino)ethane-5-tetrazole.

6. A compound according to claim 4, wherein said compound of formula I is selected from the group consisting of:

- (S)-2-(2-Heptylamino)acetic acid;
(S)-2-(2-Heptylmethylamino)acetic acid;
- 15 Methyl (S)-2-(2-heptylamino)acetate;
Methyl (S)-2-(2-heptylmethylamino)acetate;
(S)-2-(2-Heptylamino)acetonitrile;
(S)-2-(2-Heptylmethylamino)acetonitrile;
(S)-2-(2-Heptylamino)ethanephosphonic acid; and
- 20 (S)-2-(2-Heptylmethylamino)ethanephosphonic acid.

7. A compound selected from the group consisting of:

- 2-(1-Hexylmethylamino)acetic acid;
3-(2-Propylmethylamino)propionic acid;
Methyl 2-(2-propylmethylamino)acetate;
- 25 Methyl 2-(1-hexylmethylamino)acetate;
Methyl 3-(1-hexylmethylamino)propionate;
2-(1-Hexylamino)acetonitrile;
2-(1-Hexylmethylamino)acetonitrile;
3-(3-Pentylamino)propionitrile;
- 30 3-(3-Pentylmethylamino)propionitrile;

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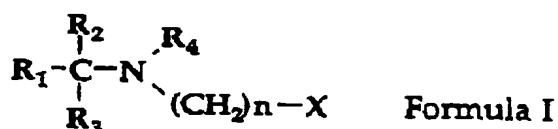
2-(2-Propylamino)ethanephosphonic acid; and
 2-(2-Propylmethylamino)ethanephosphonic acid.

8. A compound according to any one of claims 1 to 7 in the form of a hydrochloride salt.

5 9. A compound according to any one of claims 1 to 4 wherein m is an integer from 1 to 12.

10. A compound according to any one of claims 1 to 4 wherein m is an integer from 1 to 9.

11. A composition for the treatment or prevention of a disease in which cell death occurs by apoptosis, which composition comprises an effective amount of a compound having the formula I:



wherein:

15 R_1 is $(\text{CH}_2)_m\text{CH}_3$ where m is 0 or an integer in the range from 1 to 16, or an alkenyl, alkynyl, alkoxy, alkylthio, or alkyl sulfinyl group having from 2 to 17 carbon atoms, wherein R_1 may be optionally substituted with one or more substituents selected from hydroxy, aldehyde, oxo, lower acyloxy, halogen, thio, sulfoxide and sulfone,

20 $\text{R}_2 = \text{H}, \text{CH}_3$ or CH_2CH_3 ,

$\text{R}_3 = \text{H}$ or CH_3 ,

$\text{R}_4 = \text{H}$ or CH_3

$\text{R}_5 = \text{lower alkyl}$ having from 1 to 5 carbon atoms,

n is an integer in the range from 1 to 3,

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and X is carboxyl (COOH), carbalkoxy (COOR₅), cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, as a substantially pure enantiomer in the R or S configuration or a pharmaceutically acceptable salt thereof, in admixture with a suitable diluent or carrier.

5 12. A composition according to claim 11, wherein:

R₁ is (CH₂)_mCH₃ where m is 0 or an integer in the range from 1 to 16,

R₂ = CH₃,

R₃ = H,

R₄ = H or CH₃,

10 R₅ = lower alkyl having from 1 to 5 carbon atoms,

n is an integer in the range from 1 to 3,

and X is carboxyl (COOH), carbalkoxy (COOR₅), cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, or a pharmaceutically acceptable salt thereof, in admixture with a suitable

15 diluent or carrier.

13. A composition according to claim 11, wherein said compound of formula I is selected from the group consisting of:

(R)-3-(2-Heptylamino)propionic acid;

(R)-3-(2-Heptylmethylamino)propionic acid;

20 Methyl (R)-3-(2-heptylamino)propionate;

Methyl (R)-3-(2-heptylmethylamino)propionate;

(R)-2-(2-Pentylamino)acetonitrile;

(R)-2-(2-Pentylmethylamino)acetonitrile;

(R)-3-(2-Heptylamino)propionitrile;

25 (R)-3-(2-Heptylmethylamino)propionitrile;

(R)-2-(2-Pentylamino)ethanephosphonic acid;

(R)-2-(2-Pentylmethylamino)ethanephosphonic acid; and

(R)-2-(2-Heptylamino)ethane-5-tetrazole.

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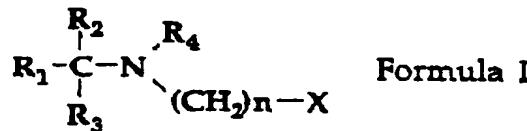
14. A composition according to claim 11, wherein said compound of formula I is selected from the group consisting of:
(S)-2-(2-Heptylamino)acetic acid;
(S)-2-(2-Heptylmethylamino)acetic acid;
- 5 Methyl (S)-2-(2-heptylamino)acetate;
Methyl (S)-2-(2-heptylmethylamino)acetate;
(S)-2-(2-Heptylamino)acetonitrile;
(S)-2-(2-Heptylmethylamino)acetonitrile;
(S)-2-(2-Heptylamino)ethanephosphonic acid; and
- 10 (S)-2-(2-Heptylmethylamino)ethanephosphonic acid.
15. A composition for the treatment or prevention of a disease in which cell death occurs by apoptosis, which composition comprises an effective amount of a compound selected from the group consisting of:
2-(1-Hexylmethylamino)acetic acid;
- 15 3-(2-Propylmethylamino)propionic acid;
Methyl 2-(2-propylmethylamino)acetate;
Methyl 2-(1-hexylmethylamino)acetate;
Methyl 3-(1-hexylmethylamino)propionate;
2-(1-Hexylamino)acetonitrile;
- 20 2-(1-Hexylmethylamino)acetonitrile;
3-(3-Pentylamino)propionitrile;
3-(3-Pentylmethylamino)propionitrile;
2-(2-Propylamino)ethanephosphonic acid; and
2-(2-Propylmethylamino)ethanephosphonic acid
- 25 in admixture with a suitable diluent or carrier.
16. A composition according to any one of claims 11 to 15, wherein the compound of formula I is in the form of a hydrochloride salt.

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17. A use of a compound of the formula I for the treatment or prevention of a disease in which cell death occurs by apoptosis, wherein said compound has the formula I:

5



wherein:

R_1 is $(\text{CH}_2)_m\text{CH}_3$ where m is 0 or an integer in the range from 1 to 16, or an alkenyl, alkynyl, alkoxy, alkylthio, or alkyl sulfinyl group having from 2 to

10 17 carbon atoms, wherein R_1 may be optionally substituted with one or more substituents selected from hydroxy, aldehyde, oxo, lower acyloxy, halogen, thio, sulfoxide and sulfone,

$\text{R}_2 = \text{H}, \text{CH}_3$ or CH_2CH_3

$\text{R}_3 = \text{H}$ or CH_3

15 $\text{R}_4 = \text{H}$ or CH_3

$\text{R}_5 = \text{lower alkyl}$ having 1 to 5 carbon atoms

n is an integer in the range from 1 to 3,

and X is carboxyl (COOH), carbalkoxy (COOR_5), cyano ($\text{C}\equiv\text{N}$), phosphonic acid (PO_3H_2), phosphonate ester ($\text{PO}_3[\text{R}_5]_2$) or 5-tetrazole, or a

20 pharmaceutically acceptable salt thereof.

18. A use according to claim 17, wherein

R_1 is $(\text{CH}_2)_m\text{CH}_3$ where m is 0 or an integer in the range from 1 to 16,

$\text{R}_2 = \text{CH}_3$,

$\text{R}_3 = \text{H}$,

25 $\text{R}_4 = \text{H}$ or CH_3 ,

$\text{R}_5 = \text{lower alkyl}$ having 1 to 5 carbon atoms,

n is an integer in the range from 1 to 3,

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and X is carboxyl (COOH), carbalkoxy (COOR₅), cyano (C≡N), phosphonic acid (PO₃H₂), phosphonate ester (PO₃[R₅]₂) or 5-tetrazole, or a pharmaceutically acceptable salt thereof.

19. A use according to claim 17 or 18 wherein the compound of
5 the Formula I is a substantially pure enantiomer in the R configuration.

20. A use according to claim 17 or 18 wherein the compound of
the Formula I is a substantially pure enantiomer in the S configuration.

21. A use according to claim 17 wherein said compound of
Formula I is selected from the group consisting of:

- 10 2-(2-Propylamino)acetic acid;
2-(1-Hexylamino)acetic acid;
(S)-2-(2-Heptylamino)acetic acid;
3-(2-Propylamino)propionic acid;
3-(1-Hexylamino)propionic acid;
15 (R)-3-(2-Heptylamino)propionic acid;
2-(2-Propylmethylamino)acetic acid;
2-(1-Hexylmethylamino)acetic acid;
(S)-2-(2-Heptylmethylamino)acetic acid;
3-(2-Propylmethylamino)propionic acid;
20 3-(1-Hexylmethylamino)propionic acid;
(R)-3-(2-Heptylmethylamino)propionic acid;
2-(2-Propylamino)acetonitrile;
(R)-2-(2-Pentylamino)acetonitrile;
2-(1-Hexylamino)acetonitrile;
25 (S)-2-(2-Heptylamino)acetonitrile;
(R)-3-(2-Heptylamino)propionitrile;
2-(2-Propylmethylamino)acetonitrile;
(R)-2-(2-Pentylmethylamino)acetonitrile ;
2-(1-Hexylmethylamino)acetonitrile;

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(S)-2-(2-Heptylmethylamino)acetonitrile;
(R)-3-(2-Heptylmethylamino)propionitrile;
2-(2-Propylamino)ethanephosphonic acid;
(R)-2-(2-Pentylamino)ethanephosphonic acid;
5 (S)-2-(2-Heptylamino)ethanephosphonic acid;
2-(2-Propylmethylamino)ethanephosphonic acid;
(S)-2-(2-Heptylmethylamino)ethanephosphonic acid; and
(R)-2-(2-Heptylamino)ethane-5-tetrazole.

22. A use according to any one of claims 17 to 21 wherein the
10 disease is selected from the group consisting of stroke, head trauma, Bell's
palsy, spinal cord injury, Alzheimer's disease, Parkinson's disease, Pick's
disease, amyotrophic lateral sclerosis, Huntington's disease, multiple
sclerosis, cardiac myopathies, nephropathy, retinopathy, diabetic
complications, glaucoma and idiopathic neuropathies.
- 15 23. A use according to any one of claims 17 to 22, for the
treatment of a human.
24. A commercial package for the treatment or prevention of a
disease in which cell death occurs by apoptosis, said package comprising a
pharmaceutical composition according to any one of claims 11 to 16,
20 together with instructions for use in the treatment or prevention of
diseases in which cell death occurs by apoptosis.